Room Temperature Stable, Dry-Transport Technology For Molecular Diagnostic Controls

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Introduction

Manufacturers of molecular controls rely on cold chain logistics for delivery of products to clinical laboratories. The controls are typically packed on dry ice and require insulated shipping containers which increases the overall cost to the end user. Additionally, if the shipment is thawed during transit it is typically replaced at manufacturer's expense. Methodology for storage and transport in a dried and thermostable format holds advantages for both manufacturers and laboratories.

To illustrate this, Alere™ recently received an FDA clearance/CLIA waiver for the *i Influenza A/B* assay which utilizes dried thermostable controls. This trend will continue with assay developers and manufacturers adopting alternate storage and shipping methods to eliminate cold chain logistics. In this study three sets of HCV controls (2 commercial, 1 lab developed) and one set of HIV controls were analyzed in their native frozen state and compared to ViveST dried, thermostable state.

Methods

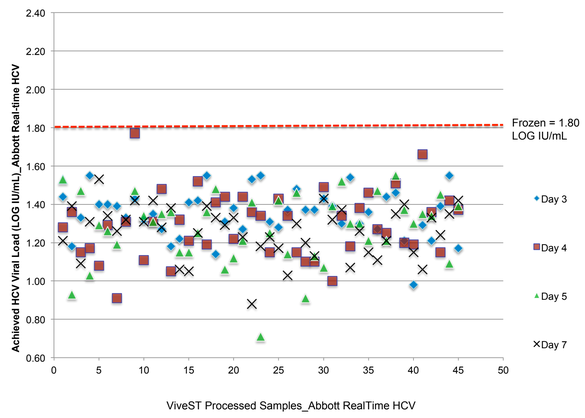
Molecular controls were loaded onto ViveST, dried overnight, capped and stored. At the time of analysis, the samples were reconstituted in a volume of molecular grade water equal to the original sample volume. Reconstituted samples were analyzed as per manufacturer package insert as outlined below:

- Qnostics Ltd (Glasgow, UK) manufactured custom HCV control material (1mL aliquots, Genotype 1b in plasma) analyzed frozen and after 3, 4, 5 and 7 days ViveST storage using the Abbott RealTime HCV Assay (ART).
- bioMONTR HCV RNA Panel (1.2 mL each, 5 levels in duplicate, n=10) were analyzed with paired frozen replicates using the Roche COBAS AmpliPrep/ COBAS TaqMan HCV Assay (TQ).
- ACCURUN 305 Series 200 and Series 400 HCV RNA Control material (SeraCare, n = 9 each series, 1 mL aliquots) were analyzed with paired frozen replicates using ART.
- An HIV-1 Genotypic Drug Resistance EQAS panel (n=5 samples) of heat-inactivated, viral culture supernatant diluted in normal human plasma (NRL, Australia) on ViveST were shipped to bioMONTR Labs and stored for 6 months analyzed with the ViroSeq HIV-1 Genotyping Assay v2.0.

Results

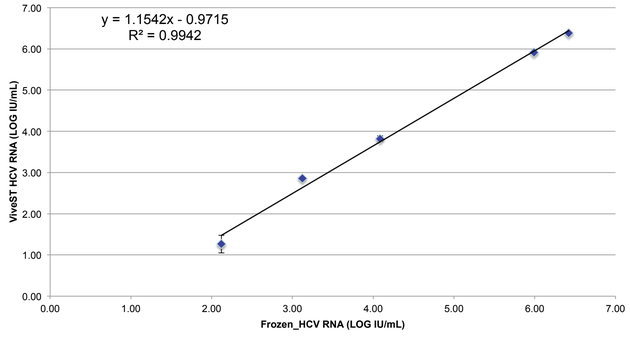
The Qnostics material (n=45 frozen) had an average viral load of 1.80 LOG IU/mL (1.56-2.20 LOG IU/mL, SD=0.17). For material recovered from ViveST, all samples were quantitated (see Figure 1) and the average viral load was 1.29 LOG IU/mL (0.71–1.77 LOG IU/mL, SD=0.16). When compared to frozen, the average reduction of HCV RNA stored on ViveST (up to 7 days) was 0.51 LOG IU/mL (ART).

Figure 1. ViveST_Abbott RealTime HCV Assay



For the bioMONTR HCV control panel, the overall Pearson coefficient among paired frozen/ViveST samples was 0.9971 (TQ). Linear regression analysis yielded an $R^2 = 0.9942$ (see Figure 2). When compared to frozen, the average HCV RNA viral load difference was -0.30 LOG.

Figure 2. bioMONTR HCV Panel_Frozen vs. ViveST

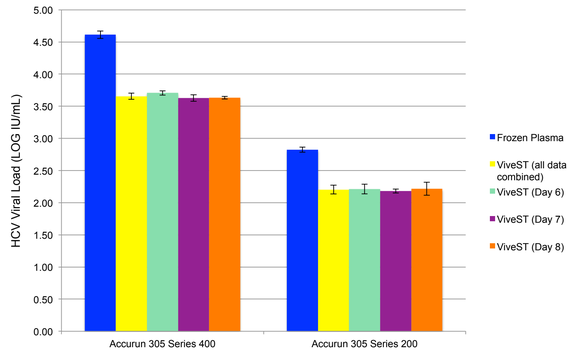


Results (cont'd)

ACCURUN 305 Series 400 panel frozen samples yielded an average HCV RNA viral load of 4.61 LOG IU/mL (SD=0.06), while samples stored on ViveST yielded an average viral load of 3.66 LOG IU/mL (SD=0.05). When compared to frozen, the average HCV RNA reduction was 0.95 LOG (ART) while the standard deviations were similar to frozen control material. Additionally, there was no significant difference in viral load between samples stored on ViveST for 6 days compared to those stored for 8 days (see Figure 3).

ACCURUN 305 Series 200 panel frozen samples yielded an average viral load of 2.83 LOG IU/mL (SD=0.04) while ViveST samples yielded an average of 2.20 LOG IU/mL (SD=0.07). When compared to frozen the average HCV RNA reduction was 0.63 LOG (ART) while the standard deviations were similar to frozen control material. Additionally, there was no significant difference in viral load between samples stored on ViveST for 6 days compared to those stored for 8 days (see Figure 3).

Figure 3. ACCURUN Panel Samples_Frozen vs. ViveST



Results (cont'd)

For the EQAS panel samples, all drug resistant mutations reported by bioMONTR Labs were present in the consensus target genotypes (TG). The drug or drug class reported was consistent with results reported by the majority of participants using the Stanford Database (27 data sets). A summary of the consensus results is provided in Table. 1.

Table 1. HIV-1 Genotypic Drug Resistance EQAS Consensus Results

In comparison with the TG develop from the EQAS Panel Results		Median performance (range) of 30 data sets	bioMONTR Labs' Performance
Agreement at the NT level:	Total(%)	98.78 (96.69 - 99.31)	98.58
	Complete (%)	100 (99.65 - 100)	99.88
	Partial (%)	98.81 (96.84 - 99.31)	98.70
Detection of:	DRM (%)	97 (89 - 103)	95
	NMs (%)	41 (18 - 79)	29

NOTES: TG = Taget Genotype, DRM = drug resistant mutation, NMs = nucleotide mixtures,

Conclusions

- ViveST can be used as storage and shipping method for molecular controls in dried, stable format that eliminates the need for cold chain storage.
- ViveST allows the amount of control material loaded to be adjusted depending on the application.
- HCV RNA recovered from ViveST provided reproducible results with SD's comparable to frozen storage.
- ViveST provides access to new and emerging markets with a method that keeps control material stable at room temperature.

References

- ACCURUN 305 Series 200 HCV RNA Positive Quality Control Package Insert (June 2011, 10084US-13)
- ACCURUN 305 Series 400 HCV RNA Positive Quality Control Package Insert (June 2011, 10086US-13)
- Qnostics Certificate of Analysis (Product Code RPBB2003-HCV 1b).
- Final Report: HIV-1 Genotypic Drug Resistance HIVG425 Panel ID: 2014-10-01 (NRL, Australia).
- Abbott RealTime HCV Package Insert (REF 1N30-90, Abbott Molecular, Des Plaines, IL)
- COBAS® TaqMan® HCV Test, v2.0 for use with the High Pure System Package Insert (P/N 05989060 190, Roche Diagnostics, Indianapolis, IN)
- ViroSeq HIV-1 Genotyping System v 2.0 and ViroSeq HIV-1 Genotyping System Software v2.8 Product Insert (REF 4J94-91)

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